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| EXAMINER | |
|---|---|
| GODDARD, LAURA B | |
| **ART UNIT** | **PAPER NUMBER** |
| 1642 | |
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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/687,035 | ALBONE ET AL. | |
| | Examiner | Art Unit | |
| | Laura B. Goddard, Ph.D. | 1642 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *30 April 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-24,26-28,44,49-53,56-62,77,103-109,116 and 117* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *26-28,107-109,116 and 117* is/are allowed.

6)☒ Claim(s) *1-24,49-53,56-62,77 and 103-106* is/are rejected.

7)☒ Claim(s) *44* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *15 October 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

### *Continued Examination Under 37 CFR 1.114*

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on April 30, 2007 has been entered.

Claims 1-24, 26-28, 44, 49-53, 56-62, 77, 103-109, 116, and 117 are currently pending and under prosecution.

### *Specification*

2. The disclosure is objected to because of the following informalities: Sections [46-48] (p. 13-14) disclose "If the antibody or antigen binding antibody fragment from such method satisfies **any one of the three embodiments set forth above** for "preferentially binds", then said antibody, or antigen-binding antibody fragment, is one that preferentially binds cell-associated CA 125/O772P polypeptide relative to shed CA 125/O772P polypeptide". It is unclear exactly what the "**three embodiments set forth above** for 'preferentially binds'" are because there are numerous embodiments preceding sections [46-48], none of which identify themselves as any of the three embodiments for "preferentially binds". Appropriate correction is required.

### *Claim Objections*

3. Claim 77 is objected to because of the following informalities: There appears to be a typographical error. Claim 77 recites the word "binds" two times in a row. Appropriate correction is required.

4. Claims 57-60 are objected to because of the following informalities: The claims are drawn to mediating 10% lysis of a *single* CA 125/O772P-positive tumor cell in an ADCC assay. It is clear that a single cell cannot have 10% lysis and Applicants intended to have multiple cells the assay. Appropriate correction is required.

5. Claim 44 is free of the art but is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

### *Claim Rejections - 35 USC § 112*

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 7-11, 49-53, and 57-60 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention. The claims recite the term "**at least about**" varying amounts of mg/ml, nM or pM, or % lysis. Using one example, it is not clear from the claims or the specification what "at least about 0.05 mg/ml" means

since 0.03 mg/ml would be "about" 0.05 mg/ml, but would not be "at least" 0.05 mg/ml. This renders the claim indefinite because the term "at least about" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. Given the above reasons, the metes and bounds of the claims cannot be determined.

7. Claim 77 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 77 recites the limitation "**the isolated antibody**". There is insufficient antecedent basis for this limitation in the claim.

### *Claim Rejections - 35 USC § 102*

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

8. Claims 1-15, 24, 49-53, 56-62, 77, and 103-106 are rejected under 35 U.S.C. 102(b) as being anticipated by WO 00/36107, Mitcham et al, published 6/22/2000 (see sequence search result # 2, Geneseq database).

The claims are drawn to an isolated antibody, or antigen binding antibody fragment, that binds to the amino acid sequence from residues 14-452 of SEQ ID No:1, wherein the antibody preferentially binds cell-associated CA 125/O772P polypeptide relative to shed CA 125/O772P polypeptide (claim 1), wherein the antibody in an ELISA competition assay, exhibits less than about 25%, 20%, 15%, 10%, or 5% inhibition of binding to the peptide of SEQ ID NO:1 in the presence of 25-fold (weight/weight) excess shed CA 125/O772P over the peptide of SEQ ID NO:1 (claims 2-6), wherein the antibody, in a flow cytometry assay, exhibits an $IC_{50}$, as measured by percent-positive cells, of at least about 0.05, 0.25, 0.5, 0.75, or 1.0 mg/ml shed CA 125/O772P (claims 7-11), wherein the antibody binds the peptide of SEQ ID NO:1, but does not detectably bind shed CA 125/O772P (claim 12), wherein the antibody is an IgG class or $IgG_1$ isotype (claims 13 and 14), wherein the antibody is monoclonal (claim 15), wherein the antibody is an anti-idiotypic antibody (claim 24), wherein the antibody binds the peptide of SEQ ID NO:1 with a $K_d$ of less than about 100nM, 10nM, 1nM, 100pM, or 10pM as measured in an antigen-antibody affinity assay (claim 49-53), wherein the antibody mediates lysis of a CA 125/O772P-positive tumor cell in an antibody-dependent cellular cytotoxicity assay (claim 56), wherein the antibody mediates at least about 10% lysis of CA 125/O772P-positive tumor cells in an ADCC assay at a 50:1, 25:1, or 12.5:1 effector:target ratio at a concentration of 5.0 ug antibody per ml (claims 57-60), wherein

the antibody mediates lysis of CA 125/O772P-positive tumor cells in a CDC assay (claim 61), wherein the antibody mediates in a range from about 15% lysis at 5ug/ml antibody to about 95% lysis at about 0.1 ug/ml antibody (claim 62), a fusion polypeptide comprising an antibody which preferentially binds cell-associated CA 125/O772P relative to shed CA 125/O772P, wherein the isolated antibody binds to the amino acid sequence form residues 14-452 of SEQ ID No:1, operably linked to a heterologous agent (claim 77), a hybridoma that secretes the antibody of claim 1 (claim 103), wherein the antibody is conjugated to a cytotoxic agent (claim 104), wherein the cytotoxic agent is a radioisotope (claim 105), and wherein the radioisotope is $^{131}I$, $^{125}I$, or $^{90}Y$ (claim 106).

Mitcham et al teach human ovarian carcinoma O772P polypeptide SEQ ID NO:388 (p. 52, line 13) that has 100% identity to amino acids 1-439 of the instant application's SEQ ID NO:1 CA 125/O772P polypeptide (see sequence search result # 2, Geneseq database). Mitcham et al teach the production of polyclonal and monoclonal antibodies that bind the polypeptide and hybridomas producing monoclonal antibodies (p. 2, lines 14-24; p. 22-23), antibody fragments (p. 23), anti-idiotypic antibodies (p. 25-26), antibodies conjugated to cytotoxic agents ricin, gelonin, and radioisotopes including, $^{131}I$, $^{125}I$, and $^{90}Y$ (p. 23-24). Mitcham et al teach the production of recombinant antibodies and linking them to heterologous agents (p. 22-25). It would be expected that some of the polyclonal or monoclonal antibodies produced would be of the IgG class or $IgG_1$ isotype.

The reference does not specifically teach that the antibodies to SEQ ID NO:388 preferentially bind cell-associated CA 125/O772P polypeptide relative to shed polypeptide, exhibit less than about 25%, 20%, 15%, 10%, or 5% inhibition of binding to the peptide of SEQ ID NO:1 in the presence of 25-fold (weight/weight) excess shed CA 125/O772P over the peptide of SEQ ID NO:1 in an ELISA, or exhibit an $IC_{50}$, as measured by percent-positive cells, of at least about 0.05, 0.25, 0.5, 0.75, or 1.0 mg/ml shed CA 125/O772P in a flow cytometry assay, or do not detectably bind shed CA 125/O772P, or bind the peptide of SEQ ID NO:1 with a $K_d$ of less than about 100nM, 10nM, 1nM, 100pM, or 10pM as measured in an antigen-antibody affinity assay, or mediate at least about 10% lysis of CA 125/O772P-positive tumor cells in an ADCC assay at a 50:1, 25:1, or 12.5:1 effector:target ratio at a concentration of 5.0 ug antibody per ml, mediate lysis of CA 125/O772P-positive tumor cells in a CDC assay, or mediate in a range from about 15% lysis at 5ug/ml antibody to about 95% lysis at about 0.1 ug/ml antibody. However, the antibody of the prior art binds amino acids 14-439 of instant SEQ ID NO:1 and it would be expected that a subset of the prior art antibodies would have the same characteristics as the claimed antibodies, absent a showing of unobvious differences. The office does not have the facilities and resources to provide the factual evidence needed in order to establish that the product of the prior art does not possess the same material, structural and functional characteristics of the claimed product. In the absence of evidence to the contrary, the burden is on the applicant to prove that the claimed product is different from those taught by the prior art and to

establish patentable differences. See In re Best 562F.2d 1252, 195 USPQ 430 (CCPA 1977) and Ex parte Gray 10 USPQ 2d 1922 (PTO Bd. Pat. App. & Int. 1989).

9. Claims 1-15, 24, 49-53, 56-62, 77, and 103-106 are rejected under 35 U.S.C. 102(e) as being anticipated by US Patent 6,468,546, Mitcham et al, filed 9/24/1999, issued 10/22/2002 (see sequence search result # 1, issued patents database).

The claims are drawn to an isolated antibody, or antigen binding antibody fragment, that binds to the amino acid sequence from residues 14-452 of SEQ ID No:1, wherein the antibody preferentially binds cell-associated CA 125/O772P polypeptide relative to shed CA 125/O772P polypeptide (claim 1), wherein the antibody in an ELISA competition assay, exhibits less than about 25%, 20%, 15%, 10%, or 5% inhibition of binding to the peptide of SEQ ID NO:1 in the presence of 25-fold (weight/weight) excess shed CA 125/O772P over the peptide of SEQ ID NO:1 (claims 2-6), wherein the antibody, in a flow cytometry assay, exhibits an $IC_{50}$, as measured by percent-positive cells, of at least about 0.05, 0.25, 0.5, 0.75, or 1.0 mg/ml shed CA 125/O772P (claims 7-11), wherein the antibody binds the peptide of SEQ ID NO:1, but does not detectably bind shed CA 125/O772P (claim 12), wherein the antibody is an IgG class or $IgG_1$ isotype (claims 13 and 14), wherein the antibody is monoclonal (claim 15), wherein the antibody is an anti-idiotypic antibody (claim 24), wherein the antibody binds the peptide of SEQ ID NO:1 with a $K_d$ of less than about 100nM, 10nM, 1nM, 100pM, or 10pM as

measured in an antigen-antibody affinity assay (claim 49-53), wherein the antibody mediates lysis of a CA 125/O772P-positive tumor cell in an antibody-dependent cellular cytotoxicity assay (claim 56), wherein the antibody mediates at least about 10% lysis of CA 125/O772P-positive tumor cells in an ADCC assay at a 50:1, 25:1, or 12.5:1 effector:target ratio at a concentration of 5.0 ug antibody per ml (claims 57-60), wherein the antibody mediates lysis of CA 125/O772P-positive tumor cells in a CDC assay (claim 61), wherein the antibody mediates in a range from about 15% lysis at 5ug/ml antibody to about 95% lysis at about 0.1 ug/ml antibody (claim 62), a fusion polypeptide comprising an antibody which preferentially binds cell-associated CA 125/O772P relative to shed CA 125/O772P, wherein the isolated antibody binds to the amino acid sequence form residues 14-452 of SEQ ID No:1, operably linked to a heterologous agent (claim 77), a hybridoma that secretes the antibody of claim 1 (claim 103), wherein the antibody is conjugated to a cytotoxic agent (claim 104), wherein the cytotoxic agent is a radioisotope (claim 105), and wherein the radioisotope is $^{131}I$, $^{125}I$, or $^{90}Y$ (claim 106).

Mitcham et al teach human ovarian carcinoma O772P polypeptide SEQ ID NO:388 that has 100% identity to amino acids 1-439 of the instant application's SEQ ID NO:1 CA 125/O772P polypeptide (see sequence search result # 1, issued patents database). Mitcham et al teach the production of polyclonal and monoclonal antibodies that bind the polypeptide and hybridomas producing monoclonal antibodies (col. 14, line 18 through col. 15, line 51), antibody fragments (col. 15, lines 52-61), anti-idiotypic antibodies (col. 2, lines 36-39; col. 17, lines 17-27), antibodies conjugated to cytotoxic

agents ricin, gelonin, and radioisotopes including, $^{131}I$, $^{125}I$, and $^{90}Y$ (col. 15, lines 62 through col. 16, line 5). Mitcham et al teach the production of recombinant antibodies and linking them to heterologous agents (col. 14, lines 57 through col. 15, line 5; col. 16, lines 6-58). It would be expected that some of the polyclonal or monoclonal antibodies produced would be of the IgG class or $IgG_1$ isotype.

The reference does not specifically teach that the antibodies to SEQ ID NO:388 preferentially bind cell-associated CA 125/O772P polypeptide relative to shed polypeptide, exhibit less than about 25%, 20%, 15%, 10%, or 5% inhibition of binding to the peptide of SEQ ID NO:1 in the presence of 25-fold (weight/weight) excess shed CA 125/O772P over the peptide of SEQ ID NO:1 in an ELISA, or exhibit an $IC_{50}$, as measured by percent-positive cells, of at least about 0.05, 0.25, 0.5, 0.75, or 1.0 mg/ml shed CA 125/O772P in a flow cytometry assay, or do not detectably bind shed CA 125/O772P, or bind the peptide of SEQ ID NO:1 with a $K_d$ of less than about 100nM, 10nM, 1nM, 100pM, or 10pM as measured in an antigen-antibody affinity assay, or mediate at least about 10% lysis of CA 125/O772P-positive tumor cells in an ADCC assay at a 50:1, 25:1, or 12.5:1 effector:target ratio at a concentration of 5.0 ug antibody per ml, mediate lysis of CA 125/O772P-positive tumor cells in a CDC assay, or mediate in a range from about 15% lysis at 5ug/ml antibody to about 95% lysis at about 0.1 ug/ml antibody. However, the antibody of the prior art binds amino acids 14-439 of instant SEQ ID NO:1 and it would be expected that a subset of the prior art antibodies would have the same characteristics as the claimed antibodies, absent a showing of unobvious differences. The office does not have the facilities and resources to provide

the factual evidence needed in order to establish that the product of the prior art does not possess the same material, structural and functional characteristics of the claimed product. In the absence of evidence to the contrary, the burden is on the applicant to prove that the claimed product is different from those taught by the prior art and to establish patentable differences. See In re Best 562F.2d 1252, 195 USPQ 430 (CCPA 1977) and Ex parte Gray 10 USPQ 2d 1922 (PTO Bd. Pat. App. & Int. 1989).

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

10. Claims 1, 13-19, and 21-24 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 00/36107, Mitcham et al, published 6/22/2000 (see sequence search result # 2, Geneseq database) in view of US Patent 5,693,762 (Queen et al, filed 6/7/1995, issued 12/2/1997) and US patent 6,136,310 (Hanna et al, filed 9/6/1995, issued 10/24/2000).

The claims are drawn to an isolated antibody, or antigen binding antibody fragment, that binds to the amino acid sequence from residues 14-452 of SEQ ID No:1, wherein the antibody preferentially binds cell-associated CA 125/O772P polypeptide relative to shed CA 125/O772P polypeptide (claim 1), wherein the antibody is an IgG or

$IgG_1$ isotype (claims 13 and 14), wherein the antibody is a chimeric monoclonal antibody (claims 15, 16 and 23), wherein the chimeric monoclonal antibody comprises a Cγ1 or Cγ4 constant region (claims 17 and 18), wherein the antibody is humanized (claim 19), wherein the antibody is bi-specific or multi-specific (claims 21 and 22), wherein the antibody is a single chain (claim 24).

Mitcham et al teach the production of monoclonal and polyclonal antibodies to human ovarian carcinoma O772P polypeptide SEQ ID NO:388 (p. 52, line 13) that has 100% identity to amino acids 1-439 of the instant application's SEQ ID NO:1 CA 125/O772P polypeptide (see sequence search result # 2, Geneseq database) as set forth above. Mitcham et al further teach using the antibodies for cancer therapy (p. 23-26; p. 33-36).

Mitcham et al does not specifically teach that the antibodies to SEQ ID NO:388 preferentially bind cell-associated CA 125/O772P polypeptide relative to shed polypeptide, however, the antibody of the prior art binds amino acids 14-439 of instant SEQ ID NO:1 and it would be expected that a subset of the prior art antibodies would have the same characteristics as the claimed antibodies, absent a showing of unobvious differences. The office does not have the facilities and resources to provide the factual evidence needed in order to establish that the product of the prior art does not possess the same material, structural and functional characteristics of the claimed product. In the absence of evidence to the contrary, the burden is on the applicant to prove that the claimed product is different from those taught by the prior art and to

establish patentable differences. See In re Best 562F.2d 1252, 195 USPQ 430 (CCPA 1977) and Ex parte Gray 10 USPQ 2d 1922 (PTO Bd. Pat. App. & Int. 1989).

Mitcham et al does not teach that the antibodies are chimeric, comprise a Cγ1 or Cγ4 constant region, or are humanized, bi-specific or multi-specific.

Queen et al teach humanized antibodies comprising CDRs from non-human donor VH and VL chains, human framework and constant regions and the humanized antibody binds the same antigen an the non-human donor antibody, providing the CDRs (see column 2-3 and 12-16, in particular). Queen et al also teach the chimeric antibodies can be bifunctional antibodies (i.e. bispecific antibodies or multi-specific), single chain, and include gamma constant regions including $IgG_1$ and $IgG_4$ (see column 11, lines 6-9 and 18-34, in particular). Queen et al teach that chimeric antibodies typically have variable segments of the genes of a mouse monoclonal antibody that may be joined to the human constant segments, such as gamma 1 (col. 11, lines 1 through col. 12, line 20; Examples 5-9; col. 11, lines 1-16). Queen et al further teach the advantages of humanized antibodies over mouse antibodies in human therapy. Because the effector portion (i.e. constant region) is human, humanized antibodies are expected to (i) interact better with the human immune system (i.e. CDC and ADCC), (ii) reduce the HAMA response and (iii) the humanized antibodies will "presumably have a longer half-life more similar to naturally occurring human antibodies, allowing smaller and less fragment doses to be given" (see column 16, lines 6-26).

Hanna et al teach that the amino acid and DNA sequences which encode human gamma 1 and gamma 4 constant domains are known in the art (col. 9, lines 1-8). Hanna

et al teach the production of chimeric, humanized monoclonal antibodies using gamma 1 or gamma 4 constant domains for therapy (abstract; col. 7, lines 60-67; col. 8, lines 45-57) and teach that using the gamma 4 domain substantially reduces Fc receptor binding, complement fixation and T cell depleting activity and exhibit enhanced stability (col. 8, lines 1-7 and 45-57; col. 9, line 65 through col. 10, line 12).

It would have been *prima facie* obvious to one of ordinary skill in the art to make chimeric, humanized monoclonal antibodies of the antibodies taught by Mitcham et al for cancer therapeutic purposes. One would have been motivated to make chimeric, humanized monoclonal antibodies as taught by Queen et al and Hanna et al in order to minimize the immunogenicity of antibody, enhance stability, and increase the half-life of the antibody for a more effective therapy. One would have a reasonable expectation of success making chimeric, humanized, or multi-specific human ovarian carcinoma O772P antibodies because methods of making chimeric, humanized, or multi-specific antibodies are well known in the art and are conventionally used.

11. Claims 1, 15, and 20 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 00/36107, Mitcham et al, published 6/22/2000 (see sequence search result # 2, Geneseq database), in view of Yang et al (Cancer Research, 1999, 59:1236-1243).

The claims are drawn to an isolated antibody, or antigen binding antibody fragment, that binds to the amino acid sequence from residues 14-452 of SEQ ID No:1, wherein the antibody preferentially binds cell-associated CA 125/O772P polypeptide

relative to shed CA 125/O772P polypeptide (claim 1), wherein the antibody is monoclonal and human (claims 15 and 20).

Mitcham et al teach the production of monoclonal and polyclonal antibodies to human ovarian carcinoma O772P polypeptide SEQ ID NO:388 (p. 52, line 13) that has 100% identity to amino acids 1-439 of the instant application's SEQ ID NO:1 CA 125/O772P polypeptide (see sequence search result # 2, Geneseq database) as set forth above. Antibodies can be produced in a variety of mammals including mice, rats and rabbits (col. 15, lines 3-40). Mitcham et al further teach using the antibodies for cancer therapy (p. 23-26; p. 33-36).

Mitcham et al does not specifically teach that the antibodies to SEQ ID NO:388 preferentially bind cell-associated CA 125/O772P polypeptide relative to shed polypeptide, however, the antibody of the prior art binds amino acids 14-439 of instant SEQ ID NO:1 and it would be expected that a subset of the prior art antibodies would have the same characteristics as the claimed antibodies, absent a showing of unobvious differences. The office does not have the facilities and resources to provide the factual evidence needed in order to establish that the product of the prior art does not possess the same material, structural and functional characteristics of the claimed product. In the absence of evidence to the contrary, the burden is on the applicant to prove that the claimed product is different from those taught by the prior art and to establish patentable differences. See In re Best 562F.2d 1252, 195 USPQ 430 (CCPA 1977) and Ex parte Gray 10 USPQ 2d 1922 (PTO Bd. Pat. App. & Int. 1989).

Mitcham et al does not teach that the antibodies are human.

Yang et al teach that monoclonal antibodies currently pursued in human clinical trials, being murine chimeric antibodies, are likely to induce immune or allergic responses to the mouse components in immunocompetent patients, which leads to reduction in the antibody efficacy and safety (p. 1236, col. 2). Yang et al teach that human antibodies can be repeatedly administered to all appropriate patient populations for cancer therapy and teaches the efficacy of a human antibody in treating cancer, the minimal immunogenicity and longer half-life of the human antibody as compared with mouse or mouse-derived monoclonal antibodies (abstract).

It would have been *prima facie* obvious to one of ordinary skill in the art to have produced human monoclonal antibodies of the antibody of Mitcham et al because Yang et al specifically teach the advantages of using human monoclonal antibodies in cancer therapy, particularly in that the use of human antibodies would reduce the immunogenic response against the antibodies during therapy and would minimize the human-anti-mouse antibody toxicity. One would have a reasonable expectation of success in using human antibodies in cancer therapy given the minimal immunogenicity and longer half-life of the human antibody as compared with mouse or mouse-derived monoclonal antibodies and success of human antibodies in treating cancer.

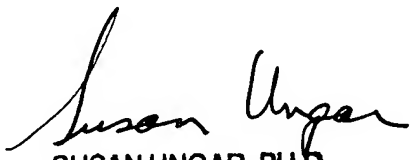
12. All other rejections recited in the Office Action mailed October 31, 2006 are hereby withdrawn.

13. **Conclusion:** Claims 26-28, 107-109, 116 and 117 are allowed. Claim 44 is objected to. Claims 1-24, 49-53, 56-62, 77, 103-106 are rejected.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Laura B. Goddard, Ph.D. whose telephone number is (571) 272-8788. The examiner can normally be reached on 7:00am-3:30pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shanon Foley can be reached on 571-272-0898. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.



SUSAN UNGAR, PH.D
PRIMARY EXAMINER

Laura B Goddard, Ph.D.
Examiner
Art Unit 1642